

## AMENDMENTS

### **In the claims:**

1. (Currently Amended) A modified antibody of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein at least one amino acid residues 250 and 428 from the heavy chain constant region selected from the group consisting of amino acid residues 250, 314, and 428 isare different from that residues present in an the unmodified class IgG antibody, ~~wherein the FcRn binding affinity and/or serum half life of said modified antibody is altered relative to that of the unmodified antibody.~~
2. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.
3. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.
4. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody is a chimeric antibody, a primatized antibody, or a humanized antibody.
5. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody is a human antibody.
6. (Original) The modified antibody according to Claim 1, wherein the unmodified antibody is OST577-IgG2M3 or OST577-IgG1.
7. (Original) The modified antibody according to Claim 1, wherein the unmodified antibody is Hu1D10-IgG2M3 or Hu1D10-IgG1.
8. (Original) The modified antibody according to Claim 1, wherein:
  - (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid or glutamine; or

- (b) said amino acid residue 428 from the heavy chain constant region is phenylalanine or leucine.
- 9. (Original) The modified antibody according to Claim 1, wherein amino acid residue 250 from the heavy chain constant region is glutamine.
- 10. (Original) The modified antibody according to Claim 1, wherein amino acid residue 428 from the heavy chain constant region is leucine.
- 11. (Original) The modified antibody according to Claim 1, wherein:
  - (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid and amino acid residue 428 from the heavy chain constant region is phenylalanine;
  - (b) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is phenylalanine; or
  - (c) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is leucine.
- 12. (Original) The modified antibody according to Claim 1, wherein said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.
- 13. (Cancelled)
- 14. (Cancelled)
- 15. (Original) The modified antibody according to Claim 1, wherein:
  - (a) said amino acid residue 250 from the heavy chain constant region is selected from the group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or

- (b) said amino acid residue 428 from the heavy chain constant region is selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine.
16. (Original) The modified antibody according to Claim 1, wherein said amino acid residue 250 from the heavy chain constant region is aspartic acid.
17. (Original) The modified antibody according to Claim 1, wherein said amino acid residue 428 from the heavy chain constant region is glycine.
18. (Original) The modified antibody according to Claim 1, wherein the modified antibody has a higher binding affinity for FcRn at pH 6.0 than at pH 7.4.
19. (Currently Amended) An antibody ~~having comprising~~ a constant region substantially identical to that of a naturally occurring class IgG antibody, wherein at least ~~one~~ the heavy chain constant region amino acid residues 250 and 428 ~~from the heavy chain constant region selected from the group consisting of residues 250, 314, and 428~~ is are different from ~~that~~ residues present in the naturally occurring class IgG antibody, and wherein the ~~FcRn binding affinity and/or~~ in vivo serum half-life of said antibody is ~~altered~~ increased relative to the naturally occurring antibody.
20. (Original) The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.
21. (Original) The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.
22. (Original) The modified antibody according to Claim 19, wherein said naturally occurring class IgG antibody is a chimeric antibody, a primatized antibody, or a humanized antibody.
23. (Original) The antibody according to Claim 19 wherein said naturally occurring class IgG antibody is a human antibody.

24. (Original) The antibody according to Claim 19, wherein:

- (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid or glutamine; or
- (b) said amino acid residue 428 from the heavy chain constant region is phenylalanine or leucine.

25. (Original) The antibody according to Claim 19, wherein said amino acid residue 250 from the heavy chain constant region is glutamine.

26. (Original) The antibody according to Claim 19, wherein said amino acid residue 428 from the heavy chain constant region is leucine.

27. (Original) The antibody according to Claim 19, wherein:

- (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid and said amino acid residue 428 from the heavy chain constant region is phenylalanine;
- (b) said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is phenylalanine; or
- (c) said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.

28. (Original) The antibody according to Claim 19, wherein said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.

29. (Cancelled)

30. (Cancelled)

31. (Original) The antibody according to Claim 19, wherein:

- (a) said amino acid residue 250 from the heavy chain constant region is selected from the group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or
- (b) said amino acid residue 428 from the heavy chain constant region is selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine;

32. (Original) The antibody according to Claim 19, wherein said amino acid residue 250 from the heavy chain constant region is aspartic acid.

33. (Original) The antibody according to Claim 19, wherein said amino acid residue 428 from the heavy chain constant region is glycine.

34. (Currently Amended) A modified ~~therapeutic or diagnostic~~ antibody of class IgG with an *in vivo* mean elimination half-life at least about ~~1.3~~1.8-fold longer than that of the corresponding unmodified class IgG antibody.

35. (Currently Amended) The modified ~~therapeutic or diagnostic~~ antibody of class IgG of Claim 34, wherein at least one of the heavy chain constant region amino acid residues 250 or 428 ~~from the heavy chain constant region selected from the group consisting of residues 250, 314, and 428~~ is different from that present in the unmodified antibody.

36. (Original) The modified therapeutic or diagnostic antibody of class IgG of Claim 34, wherein:

- (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid and amino acid residue 428 from the heavy chain constant region is phenylalanine;

- (b) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is phenylalanine; or
  - (c) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is leucine.
37. (Original) The modified antibody of Claim 34, wherein said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.
38. (Original) The modified antibody of Claim 34, wherein amino acid residue 428 from the heavy chain constant region is leucine.
39. (Currently Amended) A modified ~~therapeutic or diagnostic~~ antibody of class IgG with an *in vivo* mean serum clearance rate at least about ~~1-31.8~~ 1.8-fold lower than that of the corresponding unmodified class IgG antibody.
40. (Currently Amended) The modified ~~therapeutic or diagnostic~~ antibody of class IgG of Claim 39, wherein at least one of of the heavy chain constant region amino acid residues 250 or 428 ~~from the heavy chain constant region selected from the group consisting of residues 250, 314, and 428~~ is different from that present in the unmodified class IgG antibody.
41. (Currently Amended) The modified ~~therapeutic or diagnostic~~ antibody of class IgG of Claim 39, wherein
- (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid and amino acid residue 428 from the heavy chain constant region is phenylalanine;
  - (b) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is phenylalanine; or

(c) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is leucine.

42. (Original) The modified antibody of Claim 39, wherein said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.

43. (Original) The modified antibody of Claim 39, wherein said amino acid residue 428 from the heavy chain constant region is leucine.

44. (Cancelled)

45. (Cancelled)

46. (Cancelled)

47. (Cancelled)

48. (Cancelled)

49. (Original) A modified antibody of class IgG derived from an unmodified antibody of class IgG wherein residue 250 from the heavy chain constant region is alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, tryptophan, tyrosine, or valine.

50. (Cancelled)

51. (Cancelled)

52. (Currently Amended) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the modified antibody according to Claim 1.

53. (Currently Amended) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the antibody having a constant region substantially identical to that of a naturally occurring class IgG antibody according to Claim 19.

54. (Original) A polypeptide comprising an amino acid sequence of any one of SEQ ID NOs: 10-76.
55. (Original) A polynucleotide molecule encoding the polypeptide according to Claim 54.
56. (Original) A host cell comprising a vector comprising the polynucleotide molecule according to Claim 54.
57. (Currently Amended) A method for altering FcRn binding affinity and/or serum half-life of an antibody of class IgG comprising selecting at least ~~one~~two amino acid residues from the heavy chain constant region from the group consisting of residues 250, 314, and 428 and substituting the selected residue(s) with an amino acid different from that present in the unmodified antibody, thereby altering FcRn binding affinity and/or serum half-life of the antibody.
58. (Currently Amended) A method of producing a modified antibody of class IgG with an altered binding affinity for FcRn and/or an altered serum half-life as compared with the unmodified antibody comprising:
- (a) preparing an expression vector comprising a suitable promoter operably linked to DNA encoding at least a constant region of an immunoglobulin heavy chain in which at least ~~one~~two amino acid residues from the heavy chain constant region selected from the group consisting of amino acid residues 250, 314, and 428 is substituted with a residue different from that present in an unmodified antibody;
  - (b) transforming host cells with said vector; and
  - (c) culturing said transformed host cells to produce said modified antibody.
59. (Original) The method according to Claim 58, further comprising: preparing a second expression vector comprising a promoter operably linked to DNA encoding a complementary immunoglobulin light chain and further transforming said host cells with said second expression vector.



60. (Original) The method according to Claim 58, wherein:

- (a) said amino acid residue 250 from the heavy chain constant region is substituted with glutamic acid or glutamine; or
- (b) said amino acid residue 428 from the heavy chain constant region is substituted with phenylalanine or leucine.

61. (Original) The method according to Claim 58, wherein said amino acid residue 250 from the heavy chain constant region is substituted with glutamine.

62. (Original) The method according to Claim 58, wherein said amino acid residue 428 from the heavy chain constant region is substituted with leucine.

63. (Original) The method according to Claim 58, wherein

- (a) said amino acid residue 250 from the heavy chain constant region is substituted with glutamic acid and amino acid residue 428 from the heavy chain constant region is substituted with phenylalanine;
- (b) said amino acid residue 250 from the heavy chain constant region is substituted with glutamine and amino acid residue 428 from the heavy chain constant region is substituted with phenylalanine; or
- (c) said amino acid residue 250 from the heavy chain constant region is substituted with glutamine and amino acid residue 428 from the heavy chain constant region is substituted with leucine.

64. (Original) The method according to Claim 58, wherein said amino acid residue 250 from the heavy chain constant region is substituted with glutamine and said amino acid residue 428 from the heavy chain constant region is substituted with leucine.

65. (Original) The method according to Claim 58, wherein said amino acid residue 314 from the heavy chain constant region is substituted with a residue selected from the group consisting of alanine, arginine, aspartic acid, asparagine, cysteine, glutamic acid, glutamine, glycine,

histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.

66. (Cancelled)

67. (Original) The method according to Claim 58, wherein:

- (a) amino acid residue 250 from the heavy chain constant region is substituted with a residue selected from a group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or
- (b) amino acid residue 428 is substituted with a residue selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine.

68. (Original) The method according to Claim 58, wherein said amino acid residue 250 from the heavy chain constant region is substituted with aspartic acid.

69. (Original) The method according to Claim 58, wherein said amino acid residue 428 from the heavy chain constant region is substituted with glycine.